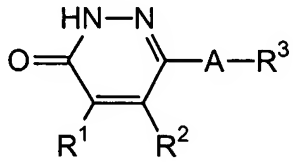
## AMENDMENTS TO THE CLAIMS

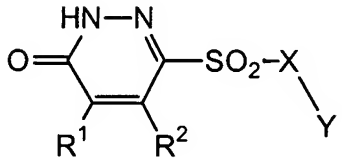
1(original). A pharmaceutical composition comprising a first compound selected from:

a compound of formula I



I,

and a compound of formula II



II,

or a prodrug of said first compound, or a pharmaceutically acceptable salt of said first compound or said prodrug,

wherein:

A is S, SO or $SO_2$;

$R^1$ and $R^2$ are each independently hydrogen or methyl;

$R^3$ is $Het^1$, $-CHR^4Het^1$ or $NR^6R^7$;

$R^4$ is hydrogen or $(C_1\text{-}C_3)$alkyl;

$R^6$ is $(C_1\text{-}C_6)$alkyl, aryl or $Het^2$;

$R^7$ is $Het^3$;

$Het^1$ is pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, quinolyl, isoquinolyl, quinazolyl, quinoxalyl, phthalazinyl, cinnolinyl, naphthyridinyl, pteridinyl, pyrazinopyrazinyl, pyrazinopyridazinyl, pyrimidopyridazinyl, pyrimidopyrimidyl, pyridopyrimidyl, pyridopyrazinyl, pyridopyridazinyl, pyrrolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, pyrazolyl, isoxazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, pyrrolopyridyl, furopyridyl, thienopyridyl, imidazolopyridyl, oxazolopyridyl, thiazolopyridyl, pyrazolopyridyl, isoxazolopyridyl, isothiazolopyridyl, pyrrolopyrimidyl, furopyrimidyl, thienopyrimidyl, imidazolopyrimidyl, oxazolopyrimidyl, thiazolopyrimidyl, pyrazolopyrimidyl, isoxazolopyrimidyl, isothiazolopyrimidyl, pyrrolopyrazinyl, furopyrazinyl, thienopyrazinyl, imidazolopyrazinyl, oxazolopyrazinyl, thiazolopyrazinyl, pyrazolopyrazinyl, isoxazolopyrazinyl, isothiazolopyrazinyl, pyrrolopyridazinyl, furopyridazinyl, thienopyridazinyl,

imidazolopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl, pyrazolopyridazinyl, isoxazolopyridazinyl or isothiazolopyridazinyl; $Het^1$ is independently optionally substituted with up to a total of four substituents independently selected from $R^8$, $R^9$, $R^{10}$ and $R^{11}$; wherein $R^8$, $R^9$, $R^{10}$ and $R^{11}$ are each taken separately and are each independently halo, formyl, $(C_1$-$C_6)$alkoxycarbonyl, $(C_1$-$C_6)$alkylenyloxycarbonyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $C(OH)R^{12}R^{13}$, $(C_1$-$C_4)$alkylcarbonylamido, $(C_3$-$C_7)$cycloalkylcarbonylamido, phenylcarbonylamido, phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, $(C_1$-$C_4)$alkylsulfenyl, $(C_1$-$C_4)$alkylsulfonyl, $(C_3$-$C_7)$cycloalkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to three fluoro or $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, in the definition of $R^8$, $R^9$, $R^{10}$ and $R^{11}$ are optionally substituted with up to three substituents independently selected from hydroxy, halo, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro and $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said imidazolyl, oxazolyl, isoxazolyl, thiazolyl and pyrazolyl in the definition of $R^8$, $R^9$, $R^{10}$ and $R^{11}$ are optionally substituted with up to two substituents independently selected from hydroxy, halo, $C_1$-$C_4)$alkyl, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $C_1$-$C_4)$alkyl-phenyl optionally substituted in the phenyl portion with one Cl, Br, OMe, Me or $SO_2$-phenyl wherein said $SO_2$-phenyl is optionally substituted in the phenyl portion with one Cl, Br, OMe, Me, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro, or $(C_1$-$C_4)$alkoxy optionally substituted with up to three fluoro;

$R^{12}$ and $R^{13}$ are each independently hydrogen or $(C_1$-$C_4)$alkyl;

$Het^2$ and $Het^3$ are each independently imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy; $Het^2$ and $Het^3$ are each independently optionally substituted with up to a total of four substituents independently selected from $R^{14}$, $R^{15}$, $R^{16}$ and $R^{17}$, wherein $R^{14}$, $R^{15}$, $R^{16}$ and $R^{17}$ are each taken separately and are each independently halo, formyl, $(C_1$-$C_6)$alkoxycarbonyl, $(C_1$-$C_6)$alkylenyloxycarbonyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $C(OH)R^{18}R^{19}$, $(C_1$-$C_4)$alkylcarbonylamido, $(C_3$-$C_7)$cycloalkylcarbonylamido, phenylcarbonylamido, phenyl,

naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, $(C_1$-$C_4)$alkylsulfenyl, $(C_1$-$C_4)$alkylsulfonyl, $(C_3$-$C_7)$cycloalkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to three fluoro or $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, in the definition of $R^{14}$, $R^{15}$, $R^{16}$ and $R^{17}$ are optionally substituted with up to three substituents independently selected from hydroxy, halo, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro and $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said imidazolyl, oxazolyl, isoxazolyl, thiazolyl and pyrazolyl in the definition of $R^{14}$, $R^{15}$, $R^{16}$ and $R^{17}$ are optionally substituted with up to two substituents independently selected from hydroxy, halo, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro and $(C_1$-$C_4)$alkoxy optionally substituted with up to three fluoro; and

$R^{18}$ and $R^{19}$ are each independently hydrogen or $(C_1$-$C_4)$alkyl;

X and Y together are $CH_2$-CH(OH)-Ar or $CH_2$-C(O)-Ar, or

X is a covalent bond, $NR^{20}$ or $CHR^{21}$, wherein, $R^{20}$ is $(C_1$-$C_3)$alkyl or a phenyl that is optionally substituted with one or more substituents selected from OH, F, Cl, Br, I, CN, $CF_3$, $(C_1$-$C_6)$alkyl, O-$(C_1$-$C_6)$alkyl, $S(O)_n$-$(C_1$-$C_6)$alkyl and $SO_2$—$NR^{22}R^{23}$, and $R^{21}$ is hydrogen or methyl, and

Y is a phenyl or naphthyl ring optionally substituted with one or more substituents selected from Ar, OH, F, Cl, Br, I, CN, $CF_3$, $(C_1$-$C_6)$alkyl, O-$(C_1$-$C_6)$alkyl, $S(O)_n$-$(C_1$-$C_6)$alkyl and $SO_2$—$NR^{22}R^{23}$;

Ar is a phenyl or naphthyl ring optionally substituted with one or more substituents selected from F, Cl, Br, I, CN, $CF_3$, $(C_1$-$C_6)$alkyl, O-$(C_1$-$C_6)$alkyl, $S(O)_n$-$(C_1$-$C_6)$alkyl and $SO_2$—$NR^{22}R^{23}$;

n is independently for each occurrence 0, 1 or 2;

$R^{22}$ is independently for each occurrence H, $(C_1$-$C_6)$alkyl, phenyl or naphthyl; and

$R^{23}$ is independently for each occurrence $(C_1$-$C_6)$alkyl, phenyl or naphthyl,

provided that when $R^3$ is $NR^6R^7$, then A is $SO_2$; and

a second compound that is a cyclooxygenase-2 inhibitor, a prodrug of said second compound or a pharmaceutically acceptable salt of said second compound or said prodrug.

2(original). A composition of claim 1 wherein said first compound is a compound of formula I, wherein A is $SO_2$; $R^1$ and $R^2$ are each hydrogen; $R^3$ is $Het^1$, wherein $Het^1$ is 5H-furo-[3,2c]pyridin-4-one-2-yl, furano[2,3b]pyridin-2-yl, thieno[2,3b]pyridin-2-yl, indol-2-yl, indol-3-yl, benzofuran-2-yl, benzothien-2-yl, imidazo[1,2a]pyridin-3-yl, pyrrol-1-yl, imidazol-1-yl, indazol-1-yl, tetrahydroquinol-1-yl or tetrahydroindol-1-yl, wherein said $Het^1$ is optionally independently substituted with up to a total of two substituents each independently selected from fluoro, chloro, bromo, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, trifluoromethyl, hydroxy, benzyl or phenyl; said benzyl and phenyl are each optionally independently substituted with up to three halo, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylsulfonyl, $(C_1$-$C_6)$alkylsulfinyl, $(C_1$-$C_6)$alkylsulfenyl, trifluoromethyl or hydroxy, or a prodrug thereof or a pharmaceutically acceptable salt of said compound or prodrug.

3(original). A composition of claim 2 wherein $Het^1$ is indol-2-yl, benzofuran-2-yl, benzothiophen-2-yl, furano[2,3b]pyridin-2-yl, thieno[2,3b]pyridin-2-yl or imidazo[1,2a]pyridin-4-yl, wherein said $Het^1$ is optionally independently substituted with up to a total of two substituents independently selected from fluoro, chloro, bromo, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, trifluoromethyl and phenyl; said phenyl being optionally substituted with up to two substituents independently selected from fluoro, chloro and $(C_1$-$C_6)$alkyl.

4(original). A composition of claim 1 wherein said first compound is selected from: 6-(3-trifluoromethyl-benzenesulfonyl)-2H-pyridazin-3-one;

6-(4-bromo-2-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(4-trifluoromethyl-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2-bromo-benzenesulfonyl)-2H-pyridazin-3-one;

6-(3,4-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(4-methoxy-benzenesulfonyl)-2H-pyridazin-3-one;

6-(3-bromo-benzenesulfonyl)-2H-pyridazin-3-one;

6-(biphenyl-4-sulfonyl)-2H-pyridazin-3-one;

6-(4'-fluoro-biphenyl-4-sulfonyl)-2H-pyridazin-3-one;

6-(4'-trifluoromethyl-biphenyl-4-sulfonyl)-2H-pyridazin-3-one;

6-(3',5'-bis-trifluoromethyl-biphenyl-4-sulfonyl)-2H-pyridazin-3-one;

6-(biphenyl-2-sulfonyl)-2H-pyridazin-3-one;

6-(4'-trifluoromethyl-biphenyl-2-sulfonyl)-2H-pyridazin-3-one;

6-(2-hydroxy-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2-chloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(3-chloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,3-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,5-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(4-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(4-chloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,3-difluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,4-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,4-difluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,6-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2-chloro-4-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2-bromo-4-fluoro-benzenesulfonyl)-2H-pyridazin-3-one; and

6-(naphthalene-1-sulfonyl)-2H-pyridazin-3-one,

or a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug.

5(original). A composition of claim 1 wherein said second compound is selected from celecoxib, rofecoxib and etoricoxib or a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug.

6(original). A pharmaceutical composition of claim 1 wherein said first compound is in an aldose reductase inhibiting amount.

7(original). A pharmaceutical composition of claim 1 wherein said second compound is present in a cyclooxygenase-2 inhibiting amount.

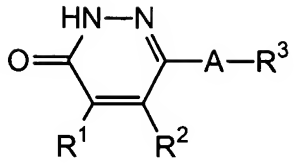
8(original). A pharmaceutical composition of claim 6 wherein said second compound is present in a cyclooxygenase-2 inhibiting amount.

9(original). A pharmaceutical composition of claim 1 further comprising a vehicle, diluent or carrier.

10-19(cancelled).

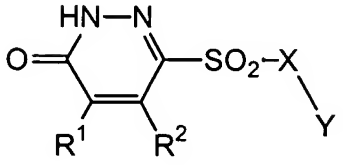
20(original). A therapeutic method comprising administering to a mammal in need of treatment or prevention of cardiac tissue ischemia a first compound selected from:

a compound of formula I



I,

and a compound of formula II



II,

or a prodrug of said first compound, or a pharmaceutically acceptable salt of said first compound or said prodrug,

wherein:

A is S, SO or $SO_2$;

$R^1$ and $R^2$ are each independently hydrogen or methyl;

$R^3$ is $Het^1$, $-CHR^4Het^1$ or $NR^6R^7$;

$R^4$ is hydrogen or $(C_1\text{-}C_3)$alkyl;

$R^6$ is $(C_1\text{-}C_6)$alkyl, aryl or $Het^2$;

$R^7$ is $Het^3$;

$Het^1$ is pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, quinolyl, isoquinolyl, quinazolyl, quinoxalyl, phthalazinyl, cinnolinyl, naphthyridinyl, pteridinyl, pyrazinopyrazinyl, pyrazinopyridazinyl, pyrimidopyridazinyl, pyrimidopyrimidyl, pyridopyrimidyl, pyridopyrazinyl, pyridopyridazinyl, pyrrolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, pyrazolyl, isoxazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, pyrrolopyridyl, furopyridyl, thienopyridyl, imidazolopyridyl, oxazolopyridyl, thiazolopyridyl, pyrazolopyridyl, isoxazolopyridyl, isothiazolopyridyl, pyrrolopyrimidyl, furopyrimidyl, thienopyrimidyl, imidazolopyrimidyl, oxazolopyrimidyl, thiazolopyrimidyl, pyrazolopyrimidyl, isoxazolopyrimidyl, isothiazolopyrimidyl, pyrrolopyrazinyl, furopyrazinyl, thienopyrazinyl, imidazolopyrazinyl, oxazolopyrazinyl, thiazolopyrazinyl, pyrazolopyrazinyl, isoxazolopyrazinyl, isothiazolopyrazinyl, pyrrolopyridazinyl, furopyridazinyl, thienopyridazinyl, imidazolopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl, pyrazolopyridazinyl, isoxazolopyridazinyl or isothiazolopyridazinyl; $Het^1$ is independently optionally substituted with up to a total of four substituents independently selected from $R^8$, $R^9$, $R^{10}$ and $R^{11}$; wherein $R^8$, $R^9$, $R^{10}$ and $R^{11}$ are each taken separately and are each independently halo, formyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkylenyloxycarbonyl, $(C_1$-

$C_4$)alkoxy-($C_1$-$C_4$)alkyl, C(OH)$R^{12}R^{13}$, ($C_1$-$C_4$)alkylcarbonylamido, ($C_3$-$C_7$)cycloalkylcarbonylamido, phenylcarbonylamido, phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, ($C_1$-$C_4$)alkylsulfenyl, ($C_1$-$C_4$)alkylsulfonyl, ($C_3$-$C_7$)cycloalkyl, ($C_1$-$C_4$)alkyl optionally substituted with up to three fluoro or ($C_1$-$C_4$)alkoxy optionally substituted with up to five fluoro; said phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, in the definition of $R^8$, $R^9$, $R^{10}$ and $R^{11}$ are optionally substituted with up to three substituents independently selected from hydroxy, halo, hydroxy-($C_1$-$C_4$)alkyl, ($C_1$-$C_4$)alkoxy-($C_1$-$C_4$)alkyl, ($C_1$-$C_4$)alkyl optionally substituted with up to five fluoro and ($C_1$-$C_4$)alkoxy optionally substituted with up to five fluoro; said imidazolyl, oxazolyl, isoxazolyl, thiazolyl and pyrazolyl in the definition of $R^8$, $R^9$, $R^{10}$ and $R^{11}$ are optionally substituted with up to two substituents independently selected from hydroxy, halo, $C_1$-$C_4$)alkyl, hydroxy-($C_1$-$C_4$)alkyl, ($C_1$-$C_4$)alkoxy-($C_1$-$C_4$)alkyl, $C_1$-$C_4$)alkyl-phenyl optionally substituted in the phenyl portion with one Cl, Br, OMe, Me or $SO_2$-phenyl wherein said $SO_2$-phenyl is optionally substituted in the phenyl portion with one Cl, Br, OMe, Me, ($C_1$-$C_4$)alkyl optionally substituted with up to five fluoro, or ($C_1$-$C_4$)alkoxy optionally substituted with up to three fluoro;

$R^{12}$ and $R^{13}$ are each independently hydrogen or ($C_1$-$C_4$)alkyl;

$Het^2$ and $Het^3$ are each independently imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy; $Het^2$ and $Het^3$ are each independently optionally substituted with up to a total of four substituents independently selected from $R^{14}$, $R^{15}$, $R^{16}$ and $R^{17}$, wherein $R^{14}$, $R^{15}$, $R^{16}$ and $R^{17}$ are each taken separately and are each independently halo, formyl, ($C_1$-$C_6$)alkoxycarbonyl, ($C_1$-$C_6$)alkylenyloxycarbonyl, ($C_1$-$C_4$)alkoxy-($C_1$-$C_4$)alkyl, C(OH)$R^{18}R^{19}$, ($C_1$-$C_4$)alkylcarbonylamido, ($C_3$-$C_7$)cycloalkylcarbonylamido, phenylcarbonylamido, phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, ($C_1$-$C_4$)alkylsulfenyl, ($C_1$-$C_4$)alkylsulfonyl, ($C_3$-$C_7$)cycloalkyl, ($C_1$-$C_4$)alkyl optionally substituted with up to three fluoro or ($C_1$-$C_4$)alkoxy optionally substituted with

up to five fluoro; said phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, in the definition of $R^{14}$, $R^{15}$, $R^{16}$ and $R^{17}$ are optionally substituted with up to three substituents independently selected from hydroxy, halo, hydroxy-($C_1$-$C_4$)alkyl, ($C_1$-$C_4$)alkoxy-($C_1$-$C_4$)alkyl, ($C_1$-$C_4$)alkyl optionally substituted with up to five fluoro and ($C_1$-$C_4$)alkoxy optionally substituted with up to five fluoro; said imidazolyl, oxazolyl, isoxazolyl, thiazolyl and pyrazolyl in the definition of $R^{14}$, $R^{15}$, $R^{16}$ and $R^{17}$ are optionally substituted with up to two substituents independently selected from hydroxy, halo, hydroxy-($C_1$-$C_4$)alkyl, ($C_1$-$C_4$)alkoxy-($C_1$-$C_4$)alkyl, ($C_1$-$C_4$)alkyl optionally substituted with up to five fluoro and ($C_1$-$C_4$)alkoxy optionally substituted with up to three fluoro; and

$R^{18}$ and $R^{19}$ are each independently hydrogen or ($C_1$-$C_4$)alkyl;

X and Y together are $CH_2$-CH(OH)-Ar or $CH_2$-C(O)-Ar, or

X is a covalent bond, $NR^{20}$ or $CHR^{21}$, wherein, $R^{20}$ is ($C_1$-$C_3$)alkyl or a phenyl that is optionally substituted with one or more substituents selected from OH, F, Cl, Br, I, CN, $CF_3$, ($C_1$-$C_6$)alkyl, O-($C_1$-$C_6$)alkyl, $S(O)_n$-($C_1$-$C_6$)alkyl and $SO_2$—$NR^{22}R^{23}$, and $R^{21}$ is hydrogen or methyl, and

Y is a phenyl or naphthyl ring optionally substituted with one or more substituents selected from Ar, OH, F, Cl, Br, I, CN, $CF_3$, ($C_1$-$C_6$)alkyl, O-($C_1$-$C_6$)alkyl, $S(O)_n$-($C_1$-$C_6$)alkyl and $SO_2$—$NR^{22}R^{23}$;

Ar is a phenyl or naphthyl ring optionally substituted with one or more substituents selected from F, Cl, Br, I, CN, $CF_3$, ($C_1$-$C_6$)alkyl, O-($C_1$-$C_6$)alkyl, $S(O)_n$-($C_1$-$C_6$)alkyl and $SO_2$—$NR^{22}R^{23}$;

n is independently for each occurrence 0, 1 or 2;

$R^{22}$ is independently for each occurrence H, ($C_1$-$C_6$)alkyl, phenyl or naphthyl; and

$R^{23}$ is independently for each occurrence ($C_1$-$C_6$)alkyl, phenyl or naphthyl,

provided that when $R^3$ is $NR^6R^7$, then A is $SO_2$,

and a second compound that is a cyclooxygenase-2 inhibitor, a prodrug of said second compound or a pharmaceutically acceptable salt of said second compound or said prodrug.

21(original). A therapeutic method of claim 20 wherein said first compound is a compound of formula I, wherein A is $SO_2$; $R^1$ and $R^2$ are each hydrogen; $R^3$ is $Het^1$, wherein $Het^1$ is 5H-furo-[3,2c]pyridin-4-one-2-yl, furano[2,3b]pyridin-2-yl, thieno[2,3b]pyridin-2-yl, indol-2-yl, indol-3-yl, benzofuran-2-yl, benzothien-2-yl,

imidazo[1,2a]pyridin-3-yl, pyrrol-1-yl, imidazol-1-yl, indazol-1-yl, tetrahydroquinol-1-yl or tetrahydroindol-1-yl, wherein said $Het^1$ is optionally independently substituted with up to a total of two substituents each independently selected from fluoro, chloro, bromo, ($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, trifluoromethyl, hydroxy, benzyl or phenyl; said benzyl and phenyl are each optionally independently substituted with up to three halo, ($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, ($C_1$-$C_6$)alkylsulfonyl, ($C_1$-$C_6$)alkylsulfinyl, ($C_1$-$C_6$)alkylsulfenyl, trifluoromethyl or hydroxy, or a prodrug thereof or a pharmaceutically acceptable salt of said compound or prodrug.

22(original). A therapeutic method of claim 21 wherein $Het^1$ is indol-2-yl, benzofuran-2-yl, benzothiophen-2-yl, furano[2,3b]pyridin-2-yl, thieno[2,3b]pyridin-2-yl or imidazo[1,2a]pyridin-4-yl, wherein said $Het^1$ is optionally independently substituted with up to a total of two substituents independently selected from fluoro, chloro, bromo, ($C_1$-$C_6$)alkyl, ($C_1$-$C_6$)alkoxy, trifluoromethyl and phenyl; said phenyl being optionally substituted with up to two substituents independently selected from fluoro, chloro and ($C_1$-$C_6$)alkyl.

23(original). A therapeutic method of claim 20 wherein said first compound is selected from: 6-(3-trifluoromethyl-benzenesulfonyl)-2H-pyridazin-3-one;

6-(4-bromo-2-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(4-trifluoromethyl-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2-bromo-benzenesulfonyl)-2H-pyridazin-3-one;

6-(3,4-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(4-methoxy-benzenesulfonyl)-2H-pyridazin-3-one;

6-(3-bromo-benzenesulfonyl)-2H-pyridazin-3-one;

6-(biphenyl-4-sulfonyl)-2H-pyridazin-3-one;

6-(4'-fluoro-biphenyl-4-sulfonyl)-2H-pyridazin-3-one;

6-(4'-trifluoromethyl-biphenyl-4-sulfonyl)-2H-pyridazin-3-one;

6-(3',5'-bis-trifluoromethyl-biphenyl-4-sulfonyl)-2H-pyridazin-3-one;

6-(biphenyl-2-sulfonyl)-2H-pyridazin-3-one;

6-(4'-trifluoromethyl-biphenyl-2-sulfonyl)-2H-pyridazin-3-one;

6-(2-hydroxy-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2-chloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(3-chloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,3-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,5-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(4-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(4-chloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,3-difluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,4-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,4-difluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,6-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2-chloro-4-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2-bromo-4-fluoro-benzenesulfonyl)-2H-pyridazin-3-one; and

6-(naphthalene-1-sulfonyl)-2H-pyridazin-3-one,

or a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug.

24(original). A therapeutic method of claim 20 wherein said second compound is selected from celecoxib, rofecoxib and etoricoxib or a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug.

25(original). A therapeutic method of claim 20 wherein said first compound is administered in an aldose reductase inhibiting amount.

26(original). A therapeutic method of claim 20 wherein said second compound is administered in a cyclooxygenase-2 inhibiting amount.

27(original). A therapeutic method of claim 25 wherein said second compound is administered in a cyclooxygenase-2 inhibiting amount.

28(original). A therapeutic method of claim 20 wherein said mammal is a human.